571-273-0729
R. KELLY

Informal copy of pending claims faxed by applicants on 10/7/04

Claims

1. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function.

2. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with a binding function comprises a receptor binding domain.

3. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain is selected from the group consisting of urokinase receptor binding domain of urokinase, receptor binding domain of epidermal growth factor, receptor associated protein that binds to LDL Receptor related protein (α_2-macroglobulin receptor) and VLDL Receptor.

4. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain comprises the aminoterminal part of urokinase which is capable of binding to the urokinase receptor.

5. A recombinant nucleic acid molecule according to Claim 2, wherein said receptor binding domain comprises amino acid residues 1 through 135 of urokinase.

6. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function is an enzymatically active domain.

7. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function has protease inhibitor activity.

8. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises a protease inhibitor or active part

thereof, said protease inhibitor being selected from the group consisting of (bovine) pancreatic trypsin inhibitor, (bovine) splenic trypsin inhibitor, urinary trypsin inhibitor, tissue inhibitor of matrix metalloproteinase 1, tissue inhibitor of matrix metalloproteinase 2, tissue inhibitor of matrix metalloproteinase 3, and elastase inhibitor.

9. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises (amino acid residues 53 through 94 of) mature bovine pancreatic trypsin inhibitor.

10. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises bovine splenic trypsin inhibitor.

11. A recombinant nucleic acid molecule according to Claim 7, wherein said domain having protease inhibitor activity comprises a tissue inhibitor of matrix metallo-proteinases.

12. A recombinant nucleic acid molecule according to Claim 1, wherein said domain with an effector function comprises (an active part of) two or more different protease inhibitors, or two or more copies of (an active part of) a protease inhibitor, or both.

13. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is selected from the group consisting of viral and non-viral vectors useful for transfection or transduction of mammalian cells.

14. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is an adenovirus vector or a retrovirus vector useful for transfection or transduction of human cells.

15. A recombinant nucleic acid molecule according to Claim 1, wherein said vector is an adenovirus vector based on shuttle vector pMAD5.

16. A recombinant nucleic acid molecule according to Claim 1, wherein said nucleic acid insertion encoding an

expressible hybrid polypeptide or protein is under the control of a cell- or tissue-specific promoter.

17. A recombinant nucleic acid molecule according to Claim 1, wherein said nucleic acid insertion encoding an expressible hybrid polypeptide or protein is under the control of an endothelial cell-specific promoter, or a vascular smooth muscle cell-specific promoter, or a liver-specific promoter.

18. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in any one of the preceding Claims to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

19. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in any one of Claims 1 to 17 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

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CLAIMS

18. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, wherein the domain with a binding function is a cell surface receptor binding domain.

19. A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian, e.g. human, cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a receptor binding domain selected from the group consisting of urokinase receptor binding domain of urokinase, receptor binding domain of epidermal growth factor, receptor associated protein that binds to LDL Receptor related protein (α_2-macroglobulin receptor) and VLDL Receptor, and a domain with protease inhibitor activity which comprises a protease inhibitor or active part thereof, said protease inhibitor being selected from the group consisting of (bovine) pancreatic trypsin inhibitor, (bovine) splenic trypsin inhibitor, urinary trypsin inhibitor, tissue inhibitor of matrix metalloproteinase 1, tissue inhibitor of matrix metalloproteinase 2, tissue inhibitor of matrix metalloproteinase 3, and elastase inhibitor.

20. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in (any one of the preceding Claims) to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

claim 18 claim 19

AMENDED SHEET

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21. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in any one of Claims 1 to 19 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

24

25

AMENDED SHEET

PATENTS

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty's Docket No: 2212.135/00

Applicant(s) : Paulus Hubertus Quax et al.

Filed : Concurrently herewith

For : Method and Construct for Inhibition of Cell Migration

PRELIMINARY AMENDMENT

Hon. Assistant Commissioner of Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination, please amend the application as follows:

IN THE CLAIMS

Please amend the following claims:

20. (amended) A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in [any one of the preceding Claims] Claim 1 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

21. (amended) A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or

transducing mammalian cells with a recombinant nucleic acid molecule as claimed in [any one of Claims 1 to 19] Claim 1 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

Please add the following new claims:

22. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in Claim 18 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

23. A process for preventing local proteolytic activity, extracellular matrix degradation, cell migration, cell invasion, or tissue remodeling, comprising transfecting or transducing the cells involved or cells in their environment with a recombinant nucleic acid molecule as claimed in Claim 19 to obtain local expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule.

24. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing

mammalian cells with a recombinant nucleic acid molecule as claimed in Claim 18 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

25. A process for producing a hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function, comprising transfecting or transducing mammalian cells with a recombinant nucleic acid molecule as claimed in Claim 19 to obtain expression of the hybrid polypeptide or protein encoded by said nucleic acid molecule, and optionally recovering the hybrid polypeptide or protein produced.

IN THE ABSTRACT

Please add the following abstract:

--Abstract of the Disclosure

A recombinant nucleic acid molecule comprising a vector useful for transfection or transduction of mammalian cells, wherein said vector contains a nucleic acid insertion encoding an expressible hybrid polypeptide or protein which comprises a domain with a binding function and a domain with an effector function. The domain with a binding function may comprise a receptor binding domain, and the domain with an effector function may have enzymatic activity, in particular protease inhibitor activity. The vector may be a viral (e.g. adenovirus or retrovirus) or non-viral vector useful for transfection or